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Patents and the Challenge of 'Open Source' in an Emergent Biological Commons
or …
The Strange Case of
Betty Crocker and The Mouse.

Abstract

Patent has long been presumed to be an essential mechanism for realising the value of intellectual labour invested in the manufacture of biological inventions. By examining how the creators of engineered mice strains deposited at the Jackson Laboratory have utilised patent, I here explore the paradoxical matter of why they have not asserted their rights in the way anticipated by patent advocates. The emergence of new open source economies in mammalian genetic resources (the Mouse Academic Commons) has served to valorise collaborative working and iterative forms of experimentation. Engineered mouse strains are, in this context, best conceived of as an experimental space or biological commons open to re-invention by all. The key issue of how individual donors can protect the integrity of their donated 'works' and capitalize on the intellectual labour invested in their creation remains, however, largely unexplored. Here I argue that value lies not in the model mouse or strain itself, but rather in the experimental techniques that assure its continued genetic integrity; and demonstrate how process patents and trademark are together deployed to assure the reliability of the personality, identity, and reputation of the protected strains; and with it the economic viability of a biotechnological commons.

(Keywords: Biological Commons, Model Organisms, Intellectual Property, Open Source, Craft, Bioinformation)

Introduction

Contemporary bioscience has become populated with a plethora of 'queer' assemblages ranging from stem cell lines and chimeras to hybridized plants and genetically modified bacteria. Although radically distinct from one another these entities could be said to share a common genealogy in that they are all understood to have been industrially 'engineered'. The supposition that these unique 'manufactures' have, in many cases, been deliberately designed and crafted for commercial use served to legitimate the view that patent protection should be made available to 'an extensive subset of animate human-made inventions' including all such engineered entities, on the understanding

that, *qua* Jefferson, ingenuity, no matter how realised, "should receive a liberal encouragement".[1]

The US Supreme Court's decision to award a patent on a genetically engineered bacterium in the 1980 Diamond *Vs* Chakrabarty [2] case saw living organisms constituted as patentable subject matter for the first time. The first patent on a mammalian organism, Harvard University's Oncomouse was granted by the USTPO seven years later.[3] The storm of domestic and international protest that attended publication of this judgement was driven by concerns that such patents contravened public morality; disrupted the 'natural order' of human animal relations and represented an escalation of patents to higher-order species. Such concerns were ultimately trumped by alternative corporate accounts that valorized the mouse's "novel physical attributes, human design and ability to assist with the study and treatment of cancer". These arguments were used to legitimate its legal institution as a "new and useful composition of matter", one to which private rights of property could lawfully obtain. As Robbins cogently argues, the Mouse "as natural animal-research tool-invention was made to *cohere*, and a logic of animal patenting established" (Robbins, 2008:27).

During the subsequent decades of the 1980s and 90s the sensibilities and practices of whole organism patenting became fully embedded in the economic rationales of the wider biomedical production complex including amongst academic institutions and

[1] As discussed in Singh, K. K. (2014). Biotechnology and Intellectual Property Rights: Legal and Social Implications. Springer. P. 28.
[2] https://supreme.justia.com/cases/federal/us/447/303/case.html
[3]The USPTO granted a patent number US4736866 to Harvard College claiming, "a transgenic non-human mammal whose germ cells and somatic cells contain a recombinant oncogene sequence introduced into said mammal".

their facilitating Offices of Technology Transfer. The passage of the Stevenson-Wydler Technology Transfer Act and the Bayh-Dole Patent and Trademark Laws Amendment in1980 generated much closer collaboration and interaction between acadaemia, corporate interests and government funded 'big science' initiatives. Patenting of research mice became normative as did the prosecution of associated rights to their use (Calvert, 2007). These typically included the imposition of reach-through restrictions on third party reproduction of the mice; field of use constraints, and royalty demands for inventions arising from their applied use. Rights that were not prosecuted formally through the application of patent where typically specified in accompanying material transfer agreements (MTAs) that established further limitations, for example on circulation of the mice or on publication of related research findings.

Commenting on these developments ten years later at the close of the twentieth century the bioethicist Sheldon Krimsky lamented that the wide spread adoption of patenting with its reliance on trade secrecy inevitably restricted the free circulation of biological and informational resources resulting in a gross privatisation of biological knowledge. When, as he argued, "every potential discovery has potential monetary value, the new culture of science will seek to protect that discovery from becoming part of the "knowledge commons" (1999: 35). In an allied argument Heller and Eisenberg similarly asserted that excessive privatization of research findings, tools and data would require prospective users to negotiate with a plethora of upstream patent holders allowing each to "set up another tollbooth on the road to product development" (1998: 698). The additional costs associated with securing permissions from multiple rights holders would, they argued, have a stifling rather than enabling effect - choking off innovation in biomedical research and engendering, in the process, a new 'tragedy of the anti-

commons'. Despite these concerns, patents proved to be a remarkably resilient and curiously promiscuous form of property protection in the biotechnological realm.

Fast forward to 2009 and we find a rather unusual article in the journal *Nature Biotechnology* by David Einhorn, then senior legal counsel at the Jackson Laboratory, (the US's premier non-profit repository for mammalian genetic resources) and his colleague Rita Heimes of the Maine School of Law. It reported that consensus had been reached within the mouse research community on the desirability of creating "a mouse commons for academic research free of concerns over patents and burdensome transactional negotiations involving licences and material transfer agreements" (Einhorn and Heimes, 2009: 890). Agreements entered into by the Jackson Lab to freely share and distribute engineered mice within academia demonstrated, they suggested, that a mouse academic commons was not 'a utopian ideal' but rather something that could work effectively in practice. These assertions raise a number of crucial, if largely under-researched, questions. How is it possible to square this embrace of 'open-sourcing' and the associated disavowal of patents with the view, widely promulgated just a decade previously, that patents were an indispensable tool for securing the prestige, reputational capital and financial reward that could flow to inventors from the manufacture of new biological 'works'? If such mice were to freely circulate without patent protection how could they be protected from unlicensed use and how would it possible for scientists who donated them to the Jackson capitalise on the investments of time, energy and technology they had invested in creating them? Taking the Jackson Laboratory's[4] model mouse strains and colonies as a case study, my aim in this paper is

[4] The Jackson Laboratory, situated in Bar Harbour, Maine, USA maintains one of the world's largest not for profit repositories of mammalian genetic resources holding over 8,000 genetically modified mouse strains which

to attempt to answer these questions by examining how the lab and its partners moved from a patenting to an open source model of biological resource exchange, and with what effects and consequences.

This then will be a paper of three parts. In the first, I examine how the engineered mice that have been crafted at, or accessioned to, the Jackson Lab have been protected under IPR law. The Jackson Laboratory is not only a repository for mammalian resources it is also home to more than 60 laboratories that perform research on key health challenges including cancer, HIV-AIDS, neurobiology and neurobehavioral disorders, and metabolic disease.[5] Researchers in these internal labs, and external researchers, sought to protect their deposited 'works' and have done so, historically, in a variety of ways. Some were patented by their authors (in this case academic research scientists), albeit for a variety of complex and sometimes counterintuitive reasons. I therefore begin my analysis by examining how those researchers who did hold patents utilized those rights. Patents have been viewed, historically, as a vehicle through which scientist inventors might secure reach through rights and royalties for commercial products developed from their protected strains, however, many did not exercise these rights to that end. What could possibly explain their unwillingness to assert their patent rights in the way Justice Berger first envisaged in 1980?

In addressing this question, I develop, in the second section, a theory about the changing ontological standing of mice models. Here I suggest that JAX®Mice mouse models are

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it distributes in over 100 countries to academic, pharmaceutical and biotechnological researchers and corporations.

[5] As outlined here: https://www.jax.org/research-and-faculty/research-labs# and here: https://www.jax.org/people/auro-nair#

perhaps best understood as collectively authored performative works rather than products *per se*. Indeed, as I argue here, the engineered mouse *itself* has become a kind of biological commons the true value of which is only fully realized through collaborative circulation and use. Patent: the extension of exclusive monopolistic rights of ownership and control can, in such circumstances, have a deadening effect on the generation of knowledge and capital. In the brave new world of the biological commons the primary work of IPR instruments is perhaps not to deliver royalties to 'inventors' but rather, as I propose here, to protect the personality, identity, moral standing and foremostly reputation of protected strains. As I argue in the third section, this work is currently being performed through the deft application of alternative forms of IPR, including trademarking and branding. These mechanisms, I suggest, play an absolutely critical, if largely overlooked role in enabling the 'open sourcing' of mammalian genetic resources and the development of much subtler but equally powerful forms of wealth creation in this emergent bioeconomy. To contextualize this analysis, I begin by providing a brief history of the production of model mice and of Jackson's unique position within that economy.

I. Manufacturing Mice

Over the past century, the mouse has developed into the premier mammalian model system for genetic research. At a molecular level mice and humans are remarkably similar with 99% of human genes having mouse counterparts or homologues. For these reasons, as Rader argues (2004:260), "it was the first mammal chosen as a 'model organism' for the human genome with its use described as a 'Rosetta Stone' for the genome's biomedical interpretation". Like humans, mice naturally develop diseases that

affect the immune, endocrine, nervous, cardiovascular and other systems, including cancer, hypertension, diabetes, osteoporosis and glaucoma. Other diseases that only afflict humans such as cystic fibrosis and Alzheimer's can be induced in mice by manipulating their genomes. This can be achieved by either inbreeding strains of mice or genetically engineering them to create mutants that will reliably acquire such diseases. Existing genes can be also selectively disabled or replaced with artificial DNA that generates genetic mutations at pre-determined genomic loci (see Hall et.al, 2009). These transgenic mice are designed to display behaviours such as anxiety or aggression or be predisposed to conditions such as alcoholism or drug addiction.

The biological properties of the mouse: tameness and user friendliness, its small size, high natural mutability and fecundity make it an ideal tool for experimental biomedical research that requires large sample sets or involves the observation of generational patterns of genetic and phenotypical expression. Previous work (Löwy and Gaudillière 1998, Rader, 2004; Kirk, 2008) has outlined the enormously complex social and material practices that have attended the transformation of the mouse from 'wild' creature to highly standardised model organism capable of being reproduced with the least possible variability across generations. As Ankeny and Leonelli have noted (2011:316) processes of standardisation and the establishment of 'pure lines' are key to genetic research as they allow "features valued by researchers to be reproduced with the least possible variability across generations" thus providing "a detailed genetic account of the standard organisms in terms of sequence, gene function and phenotype". In the post genomic era however, the ability or even the desirability of making mouse strains 'sit still' indefinitely is, as Davies (2013) argues, increasingly questioned – a matter to which I shall return shortly.

From its establishment in 1929, The Jackson Laboratory (hereafter JAX, as christened by its research staff) and its founder Clarence Cook Little played a central role in the production of the first genetically standardized mice and inbred mouse strains including spontaneous and induced mutants. Driven initially by Little's personal interests in mammalian genetics and cancer research, the demand for stabilised lines on which to perform consistent comparative work with the least possible variability began to increase as their experimental utility was confirmed. Much has been made in recent accounts of the scaling up of mutant mouse production that consequently occurred at JAX during the pre-war Fordist period. Rader for example, reminds us that JAX's facilities became cast in the public imagination as 'mouse factories' where strains were 'mass produced', a notion that greatly appealed to its corporate funders such as Detroit car manufacturers, The Hudson Motor Car Company (Rader, 2004:20). Corporate embrace of intellectual property rights and the resultant increase in the patenting of inventions during this era of US industrial development certainly acted to provoke debate on whether mutant mice might also be protected as alienable 'compositions of matter' or 'manufactures'.

This narrative gained purchase throughout the post war period as techniques for molecular level manipulation were refined and as researchers and their financial backers sought new means to capitalise on their investments in research. The conception that engineered organisms are an embodiment of a set of ideas about how to re-design nature manifest in a material form, crystallised during the late 1960s along with the concomitant assertion that, as 'inventions' they ought rightfully be subject to mechanisms of IPR protection, notably patent. The precedent setting Diamond *Vs*

Charabarty decision which had, for the first time, legitimated the patent of a genetically engineered bacterium as a "non-naturally occurring manufacture or composition of matter",[6] precipitated the patenting of higher forms of life culminating in Harvard's patent for their 'man-made model system for the study of cancer', the OncoMouse (Kevles, 2002: 84) [7].

Whilst Harvard held the patent they were also obliged to fulfil obligations to their funders, the Dupont Corporation, which had invested six million dollars into development of the mouse. This investment was to be returned by giving Dupont exclusive rights to license and extract royalties from applied uses of the mouse. In anticipation of forthcoming marketisation and sales the mouse was also given a registered trademark: OncoMouse®. However, Paul Clark, Harvard's principle patent counsel made clear at the time that he believed that "the work's most apparent and compelling manifestation *was the animal itself*" (my italics). He was also certain that method patents on the means of production for the mouse would not suffice: "that it was better to protect the product as well as the processes used to produce it, otherwise competitors using different processes, could develop similar products" (cited in Kevles, 2002:84). It is worth noting here the clear assertion that it is *the mouse itself* that constitutes the intellectual property that patent is called upon to protect.

[6] It is important to note that the fundamental principle established in the Diamond *Vs*. Chakrabarty case: that the mere isolation of genes was sufficient intellectual labour to warrant patent protection was later overturned in the landmark case Association for Molecular Pathology *Vs*. Myriad Genetics (2013).

[7]The OncoMouse patent was later subject to considerable contestation in European and Canadian jurisdictions on the grounds that its passage would be contrary to "ordre public" or morality. The Supreme Court of Canada rejected a patent on OncoMouse by a majority in 2002 after determining that the mouse did not constitute a 'manufacture or composition of matter within the meaning of invention'. The patent has since been revoked or expired in several jurisdictions including the US and Europe.

Deeply held concerns about the implications that patenting could have for delimiting access to vital mouse strains erupted publicly at the Mouse Molecular Genetics meeting at Cold Harbour in 1992. At this meeting Harold Varmus's then Director of the NIH made an impassioned plea for maintaining unfettered academic access to model mice to advance biomedical research for the public or common good (Paigen, 1995). This call was taken up by Dr. Kenneth Paigen, then Director of JAX who announced that the lab was prepared to act as a repository for all new strains of inbred and genetically modified mice generated in the US. The philosophy of the repository[8], which became known thereafter as the Induced Mutant Resource or IMR, was to accept all genetically engineered mice, whether patented or not, and to then distribute them for use to academic institutions, pharmaceutical and biotech companies worldwide for research purposes, unfettered by onerous licensing requirements such as reach through or royalty rights. Individual researchers who developed mutant mice strains in the late 90s and early 2000s in the US had particular interests in ensuring that their mice were deposited for distribution with a central well organised repository. Although many strains would ultimately have only limited distribution they nevertheless remain crucially important to particular biomedical research projects and all researchers wished to make them available to maximise their utility to any prospective user.

Researchers who were unable to shoulder the costs of maintaining, characterising or distributing these strains themselves appreciated JAX's willingness to take on these responsibilities for them. However, whilst JAX could charge a fee for reproducing the mouse itself on demand; this alone could not capture the full value of the animal as a

[8] Repository mice include inbred strains, strains and stocks carrying either induced or spontaneous mutations, strains and stocks carrying chromosomal aberrations, recombinant inbred strains, recombinant congenic strains, chromosome substitution (consomic) strains, and congenic strains (strains with selected alleles maintained on specific genetic backgrounds).

research tool. Financial compensation for the intellectual labour invested in generating them could only be secured through additional use licensing that Jackson could negotiate with for profit entities (such as pharmaceutical and biotech companies) on the inventors' behalf. It might be presumed, therefore, that the majority of the researchers who deposited strains with Jackson would seek to patent them and to secure royalties for their subsequent use, this was certainly, at that time, the wider normative presumption about how animal patenting should work. To test this theory JAX's then senior legal counsel David Einhorn joined researchers at the Maine School of Law to undertake a retrospective assessment of how patent performed in these years (Einhorn and Heimes, 2009). Their intention was to establish the extent of patent adoption and to determine to what degree patent might have inhibited dissemination and ultilisation of the mice and, thus, downstream development of proprietary products based on those mice.

The results showed that some 70 researchers had contributed unpatented mouse strains to the repository. Unsurprisingly, none had sought to impose any "reach-through", internal breeding or field-of-use restrictions for academic recipients although most (92.8%) had required for-profits to sign a licencing agreement of some kind. What their research also revealed however, was that none of the donors of *patented* strains had sought to impose any substantive restrictions, reach through rights or royalty provisions on prospective users either. In other words, as Einhorn and his team concluded "licenses were nearly universally free from any substantive restrictions on downstream academic research, *whether or not the mouse strain was patented,* leaving researchers free to develop and commercialise downstream inventions made in the course of research use of the mice" (Einhorn and Heimes, 2009: 891). In other words,

the anti-commons effect of patent was, in practice, decidedly weak. Why did all of these 'inventors' not, as predicted, acquire patents to their engineered mice or use them to prevent others from capitalising on their inventions without suitable compensation? It is to an examination of these questions that we now turn.

II. The mouse as collectively authored, performative 'work'.

To understand why patent proved to have so little bearing on negotiations over the prospective circulation and use of these model mice it is essential to understand how model mice have been conceptualised ontologically; characterised and employed in research settings and how the dynamics of their production has evolved over time. Unlike other early twentieth century examples of industrial inventorship and manufacture, attempts to create genetically stable inbred mouse colonies were not singular endeavours but rather relied from the beginning on sustained collaborations between a highly variegated community of 'mouse fanciers'. Ontological distinctions between 'scientific' breeders and local dilettantes were not initially as formally constructed as they were destined to become and the establishment of the first collections of such mice were produced out of an economy of fluid exchange between the two constituencies. Local mouse fancying organisations were extremely popular in the US in the 1920s but nowhere more so that in New England. Fanciers bred specimens to exhibit particular 'standard' features in reliably replicable ways but also selected those with desirable traits such as distinct coat markings or behaviours, creating unique strains that they showed around the country.

As Rader (2004: 32-3) notes, Clarence Little and colleagues drew heavily on stocks generated by these fanciers as they had already "essentially routinized the activity of mouse breeding in captivity well before scientists became interested in the mouse as an experimental organism". Amongst these fanciers was Abbie Lathrop who had first observed skin lesions on some of her own inbred mouse strains as early as 1908 and who went on to elucidate the link between hormones and cancer susceptibility by 1916 through the methodical production of 'cancerous families of mice'. Although over time such colonies were imported into Jackson becoming there concentrated and stabilised they are best understood both then and now not as the manufactured outputs of corporate mass production but rather as Richard Sennett (2008: 33) describes it "the experimental mark of technological craftsmanship".

Naturally occurring mouse mutants arise only infrequently, and mouse geneticists were at this time seriously hampered by a lack of such resources. It is interesting to note that Rader goes on to describe the organisation of mouse genetic work in 1920s America as proceeding "in an almost guild like fashion … that was predicated on an extended one on one apprenticeship with the master professor himself" (Rader,1998: 340). The creation of extended networks of communication and exchange between graduates set the rules for "an original communal culture" and "ecology of knowledge" (1998: 333-8) that valorised sharing of resources and fine craft working. The ethos of craftsmanship: that of 'making things well' and of 'doing good work for its own sake' is built, as Sennett argues, around a particular set of open ended and iterative practices. As he suggests, when "practice is organised as a means to a fixed end, the problems of a closed system reappear: the person in training will meet a fixed target but won't progress further. An open relation between problem solving and problem finding, as in Linux work, builds

and expands skills but this can't be a one-off event. Skill opens up in this way only because of the rhythm of solving and opening up, that occurs again and again" (Sennett: 2008: 37).

It is significant that Sennett here contemporises understandings of what constitutes craftsmanship by relocating that tradition within high tech industries such as computer software generation, as practised by the Linux community. In explicating the social dynamics that underpin such work Sennett goes so far as to argue that "good craftsmanship implies socialism" that it "depends on curiosity, tempers obsession; that craftwork turns the craftsman outwards," into continued engagement with other specialists within and beyond local workshops (2008: 288). Mouse researchers later followed this edict in crafting their highly engineered strains, drawing on formal and informal expertise from New England and beyond; the unfettered circulation of strains domestically and internationally; and the open exchange of highly characterised genetic sequence information. The resultant colonies of mutant mice that are now centralised at JAX are a resource that has, it could be said, been collectively authored over time through a sustained work of distributed labour.

The collectivised and iterative nature of this form of manufacture was clearly evidenced in aftermath of the fire of 1947 that devastated the Jackson Lab and its resident mouse colonies. Rebuilding these stocks would have been impossible had many thousands of researchers located in the US and beyond not responded by sending back to Jackson breeding pairs of mice that they previously received. In the 1980s, researchers at JAX began to analyse genetic mutations within these distributed colonies mapping them to construct the Lab's Mouse Genome Database which is, in turn, continually referenced by

researchers generating new strains (OECD, 2001: 20). Maintaining access to these resources became a key modality of life within the mouse genetics research community an ethos that underpinned their public commitment to the generation of one of the world's first biotechnological commons: their Mouse Academic Research Commons or Mouse Commons. The question of how to defend access to these resources was a complex one and involved the inventive use of a variety of existing IPR mechanisms, including initially, and curiously enough, patent itself.

Defensive Patenting and the Biological Commons

In a compelling retrospective analysis of the use of patent in molecular genetics and more specifically in the production of engineered mice, Fiona Murray provides a nuanced account of their adoption amongst various and, some might well imagine, opposing constituencies. Complicating the obvious narrative of corporate embrace and academic rejection of biological patenting, she reminds us that many of the academic scientists that were expressing outrage at the restrictions the Dupont corporation were imposing on use of the Oncomouse (including prohibition of sharing or breeding extensively from the mouse) were simultaneously beginning to patent their own transgenic mice. In many instances their aim was political rather than economic. Academic scientists were learning that they could employ patents to prevent corporate acquisition of their work, establish their own terms and conditions of exchange, and thus create an open academic research commons by effectively "excluding the excluders" (Murray, 2010: 368). Patent was being enrolled to perform two particular kinds of work in generating and maintaining this nascent biological commons. As Lezuan and Montgomery (2015: 15) explain, rather than being used as a singular piece

of IP it was instead being deployed "as an attractor to bind diverse interests to a shared mission", by demarcating "a set of valuables" (in this case their patented mice) that they could "keep out of circulation and the intensification of exchange." They were, in this sense, using "the constrains traditionally imposed by intellectual property rights in order to usher in a new era of 'open innovation'" (Lezuan and Montgomery, 2015: 4).

Over time however, JAX researchers began to recognise that the creative and thus economically generative potential of the alterations that were being made to the mice could only be fully realised when they were collaboratively witnessed, shared and cooperatively refined. Exclusion, even when performed defensively, did not facilitate this end. A genuinely comprehensive and widely accessible mouse commons could only emerge if the "open sourcing" of mammalian genetic resources were to become a reality. The term 'open source' is drawn deliberately from the informational domain in order to point up parallels between the digital informational economy and the bioeconomy in relation to their use of what might be termed *foundational programmatic resources*. These are resources (whether informational or corporeal) that can, at a fundamental level, be creatively and iteratively re-programmed to produce from them new products or process that are, in their turn, scientifically, technologically or economically productive.

In the digital realm this would include "source code" which, under open source software licensing, has been published and made available to the public enabling them to copy, modify, reengineer or even redistribute it without paying royalties or fees. Such users are encouraged to access it without the restrictions of a patent regime in order to produce from it, other products via what Castells would refer to as a 'cumulative

feedback loop'. In the biological realm these kinds of foundational programmatic resources may include DNA, databased sequences or even whole organisms such as engineered mice (Deibel, 2014). All can be viewed as enabling technologies that can and should be copied, modified, re-engineered or re-distributed without imposition of reach through rights in the service of the generation of further (patentable perhaps) products. Early models that promoted open access include the Bermuda Principles that established rules for the rapid accessioning and release of the Human Genome Project DNA sequence data and the agreement by drug companies in the Single Nucleotide Polymorphism Consortium to deposit their bio-information in the public domain. Each realize the concept of 'open source biology' by making bio-informational technologies and sequences that would otherwise be the subject to restrictive intellectual property rights regimes available to scientists without restriction.

Whilst a share-waring commons ethos is now emerging as a key mode of exchange within the life sciences, proprietary modes of ownership have not disappeared altogether. Rather, as a number of scholars have recently noted, open and closed models of innovative now often co-exist; albeit in sometimes contradictory and uneasy ways (Calvert, 2012; Leonelli, Spichtinger and Prainsack, 2015; Lezuan and Montgomery, 2015; Nelson, 2018). The question of how to realise the value of embodied intellectual labour when the 'product' is freely circulated and able to be reproduced elsewhere was certainly one that began to exercise the minds of JAX's community of researchers. How could they make a commons model of open access to biological resources work in practice? This raises an important, but often under theorised, question: *what is it* that is requisite of protection in this new biological commons, and how might that protection best be effected? In answering that question I want to argue here that it is no longer the

mouse itself, as a singular organism or piece of embodied property that authors seek to protect but rather *the brand* - the identity and personality - of their mouse strains that they hope to shield from besmirchment. I argue in the following sections that this kind of protection is most effectively secured through the application an older form of intellectual property right that has, to date, played a much less celebrated but I would argue no less significant role in realising the new biological commons, namely, trademark.

The mouse as operative environment

The need to protect 'manufactures' as alienable *product*s makes sense in circumstances where use of the product results in its depletion or ultimate consumption, as the inventiveness that is invested in realizing the product must be rewarded before the product itself is exhausted. Licenses to produce patented commodities such as laptop computers or post-it notes fulfill this function, returning royalties for production and sale. This ethos informed the earliest approaches to protection of biological works in the biotechnological realm and resulted in the grant of patents to whole engineered organisms that were understood and protected as single inventions or 'products'. This is because patent law can only take account of inventions that are specific 'things' with applied uses; it is constitutionally forbidden in the US and other jurisdictions to provide monopolistic protection for products of nature, abstract ideas, information, or discoveries. Consequently, as Carolan argues (2010), the primary work performed by the patent law system in the US at this time was to purify and stabilize the identity of biological inventions; to extract them from the hinterland of the wild, messy natural

world in which they were previously contextualized (unpatentable territory) and to render them as immutable, ontologically distinct, objects.

Whilst a great deal of effort has been invested in perfecting this process of ontological purification its success was only partial. Two factors contrived to complicate the patent examiners' work. Firstly, it proved difficult to construct or patrol distinctions between patentable and unpatentable elements of particular organisms. This resulted in some surprising rulings including in the case *Monsanto Canada Inc. v. Schmeiser,* [9] in which the majority arrived at the view that patented genes or cells, when introduced into an organism, would serve to extend patent protection to that whole (previously unpatented) organism. This clearly generated considerable impediments for researchers, particularly those in the emerging field of synthetic biology, who wished to work experimentally with what the Court, in its judgement, described as 'these Lego blocks'. Drew Endy, a leading synthetic biologist had already begun to construct a technological catalogue of 'biocomponents' (Endy, 2005) or 'plug and play' biological building blocks from which could be assembled a variety of novel biological entities. Obliging prospective users to secure licenses and/or pay the rights holder royalties for each subsequent use of this componentry would add transactional costs that were wholly prohibitive.

These concerns were particularly pressing for mouse researchers. The number and

[9] Percy Schmeiser and Schmeiser Enterprises Limited v Monsanto Canada Incorporated and Monsanto Company[2004] 1 S.C.R. 902, 2004 SCC 34 at 156. available in full at *Journal of Environmental Law* (2005) 17 (1) pp. 83-108. Available at https://pdfs.semanticscholar.org/7a91/647d60ec1e97f1b66651d38d85a1611aea01.pdf

diversity of mouse models they were experimenting with had begun to proliferate in direct response to the need to develop ever more specialized 'platforms' for analyzing a multiplicity of gene-phenotype relations. The emergence of system genetics - the study of interactions among the genes in a biochemical pathway – required those conducting mouse-based biomedical research to construct new tools. The sequencing of the human and mouse genomes enabled researchers to elucidate the function of particular genes but expediting this research required the generation of what are termed 'knockout mice': those in which specific genes are either removed or disrupted. However, this task was complex and by 2004 less than10% of the 25,000 mouse genes had been removed in engineered mouse models (Austin, et.al, 2004). The ambition became to create from one inbred strain a comprehensive genome-wide resource of mutant embryonic stem cell lines[10] each of which would have a different gene knocked out.

There was an immediate recognition that this could not though be achieved unless researchers had unfettered access to the genes and technologies that were central to mutant mouse production, and if the resultant knockout mice could then be freely circulated to researchers to further experiment on. The full utility of these new models could only be realised by creatively and freely re-working the constituent elements of the founder strains' chromosomal architecture. A clear impediment to this aim was the fact that many of these modified genes; technologies and processes were already patented. One potential remedy proposed at the time of inception was that the newly formulated KnockOut Mouse Project or KOMP consortium (a multiply constituted, geographically dispersed team of researchers)[11] resolve existing patents claims through

[10] That could be cryopreserved and later generated into whole, experimental, knockout mice.
[11] This is another iteration of collaborative craft working.

the creation of a novel "'patent pool', similar to that then being developed for use in the semiconductor industry" (Austin et.al. 2004: 923)

A further issue that complicated the application of patent in this domain was the difficulty of pinning down the 'thing' to which a patent right might be due. Despite legislative attempts to narrate a stable identity for these biological inventions their liveliness and replicability made it difficult to guarantee that the modified strain to which a product patent pertained would remain consistent over time. This mutability also created technical difficulties for researchers within the lab and beyond. For what is significant in such a vitalist laboratory is what has always been essential for experimental practice: conditions of consistency, stability, and standardisation, as each provide vital defences against the scientist's nemesis: the unknown variable. Model organisms are developed (often collaboratively) out of experimentation but once refined they must then be stabilised if further applications and uses of the mouse are to have a consistent 'control'. As Leonelli *et.al* (2014) have noted, the wider empirical context in which they are deployed can also affect model validity. Even stabilised model organisms need to be understood as thoroughly 'situated' as they are constantly responding to environmental stimuli and the material conditions in which they find themselves. In this sense they cannot be thought to exist as 'stand-alone' models for human behaviour but rather gain validity only when placed in particular empirical contexts. Standardisation of environmental background and modified strain have thus become extremely important in model organism research. If both cannot be reliably reproduced without random variability there can be no valid basis for meaningful hypothesis testing or vital

comparative studies.

It thus became evident that it had become wholly unproductive to view model mice simply as 'tangible products' there to be maximally commercialized without regard to the impact monopolisation may have on other researchers. Rather than being seen as a finished 'product' to be covetously controlled as a single piece of tangible intellectual property, the engineered mouse and mouse model colonies from which they are drawn became constituted not just as a set of essential research tools, but rather as a vital experimental space or *operative environment* within which to continually experiment on the 'software' of mammalian genetics and phenotypical associations (see also Davies, 2012; 2013). In order to explicate all the changes that are induced in the mouse through each experiment they need to be bred again to establish the effects of removing or reintroducing a particular set of genes back into an otherwise fully stripped down immune system. Attempting to exert patent rights to every resultant organism became both untenable and undesirable.

Consistency is a key quality of many operative environments such as computer program platforms (viz Sennett's Linux). The stability of the platform provides each author with a referential anchor but must therefore, be capable of being widely circulated and reproduced time and again with no loss of fidelity. This provides the essential 'common ground' for communal experimentation. Whilst computer program platforms are amenable to this kind of replication, mice, though humble creatures, are not so deferential. Even engineered mouse populations that are essential 'clonal' cannot be reproduced endlessly with absolute consistency. A significant problem that can occur is

'genetic drift'.[12] Some arising and unintended mutations are immediately evident others are more subtle and difficult to detect and this is highly problematic for researchers. Over time the 'identity' the 'personality' we might even say of the mouse model will change – it will become, in effect, a poor copy of its itself, one riven with inconsistencies, corrupted, polluted, dissolute. What is at risk when this occurs is the *reputation of the strain, and with it, the reputation of the JAX Brand.*

I would argue that JAX has long understood (albeit perhaps intuitively) the importance of brand identity and reputational capital in building stable markets for this kind of 'biological software'. Conceiving of it as such also helps to explicate why Jackson has shown comparatively little interest in supporting the patenting of engineered mice as finished 'products'. They have instead, as I shall argue here, preferred to build and protect an unassailable reputation for the fidelity and stability of their mouse strains as a foundational informational resource - a form of source code, if you will, on which others can reliably experiment. They have done so via the deft application of another IPR mechanism, patent's much less well recognised cousin: trademark. As I will argue in the final sections of this paper, in so doing they have created an enviable brand identity and standing for their mouse strains and have thus managed (on behalf of their contributors) and even in the absence of what were assumed to be essential product patents, to create an economically viable open source economy in mammalian genetic

[12] Genetic drift describes random fluctuations in the numbers of gene variants in a population and takes place when the occurrence of variant forms of a gene, called alleles, increases and decreases by chance over time. It usually occurs in small populations, where infrequently occurring alleles face a greater chance of being lost. Once it begins, genetic drift will continue until the involved allele is either lost by a population or until it is the only allele present in a population at a particular locus. Both possibilities decrease the genetic diversity of a population.

shareware.

III. Betty Crocker and the Mouse: Trademark and protection of brand identity

Protection of brand identity has a long history in corporate development. Historically the trademark performed the function of associating manufactured goods with their owners and originators. As Schecter (1925:21) notes in his seminal treatise on the history of trademarks, until the early medieval period the trademark performed a dual function as both "personal or proprietary mark' and 'production mark' assuring the quality of the good through direct association with the personal qualities or identity, indeed the reputation, of the maker". As I hope to have explicated here, model mouse development at Jackson had its genesis within a tradition of crafted production amongst mouse fanciers that was itself located within a wider heritage and economy of craftworking and craftsmanship that existed in Maine at that time.[13] The earliest strains of inbred mice that were accessioned to Jackson were very much a product of this tradition in the late 1930s. The advent of mass production typically results in the detachment of the maker (him or herself) from the manufactured product. At this point reputation comes to subsist in the corporate identity of the brand. For example, once Coco Chanel stopped making her collections herself, the name Chanel (as trademark and brand) came to serve as the carrier of her reputation (Marvel, 2008). Trademarks have thus come to serve a number of vital economic functions: they are used to establish the provenance (source of origin of goods or service); to encapsulate complex, but unobservable information about the quality or characteristics of said products at a

[13] I am indebted to Sarah Franklin for reminding me of this fact.

glance; and to reduce a consumer's search costs by, lastly, allowing them to distinguish 'reputable' products from others, with relative ease.

Trademarks differ from product patents in important ways that are of relevance to this argument. It may appear that patents more effectively support the public good function of IPR law in that they encourage (ultimately) disclosure of knowledge about the evolution of methods of production and prevent others from free riding on the intellectual labour of inventors by preventing unlicensed reproduction of their work. Trademarks may appear at first to be less exclusionary as they do not attempt to restrict this kind of unlicensed copying – competitors can reproduce the work, just not under the same brand. Yet, as the World Intellectual Property Organisation has recently noted "the brand may be all that matters: when trademarks protect brands with significant reputational value, the brand, *in and of itself*, becomes a product characteristic that consumers care about but that competitors cannot copy" (WIPO, 2013: 86). In this sense it becomes perhaps the most sophisticated mechanism for protecting IPR in the commons environment.

In some instances, trademarks themselves are allowed to evolve spontaneously over time. An example of a corporate brand that has undergone its own kind of 'genetic drift' is that of the iconic American cake maker, Betty Crocker. Beginning as a stereotypical WASP in 1933, Betty's identity has been progressively reinvented to reflect the changing genetic constitution of those identified as consumers of the brand, morphing slowly to become variously more Afro Caribbean, Asian and Indian (See Fig. 1 and also Marks, 2007). This is a transmutation that has produced economic value for the company who have utilised it to continually update and refresh their brand. More

typically though, corporate producers work to maintain consistency in brand identity, and to ensure that unlicensed manufacture of inferior copies of their product does not tarnish the reputation of their brand. Brasso and Coca Cola both provide good examples of the perceived importance of maintaining the integrity and consistency of a product; its trademark and associated reputational capital. (see Fig. 2).

From its inception, but particularly given concerns raised over the constraining effect that patents could have on research activity, Jackson had articulated an institutional commitment to circulate inbred or engineered mice free of patent and licensing demands. As C.C. Little was to comment retrospectively: "we could have monopolised these mice …we could have sent out only mice of one sex or strain but we said … 'we shall share these mice with everybody that we can' (cited in Rader, 2004: 257). From the 1930s onwards, JAX began to supply mice to a wide range of users for research and general medical use, but from 1938 onwards also began to produce codified compendiums of highly detailed biological information about these strains. This effectively stabilized and made accessible tacit information formerly shared only amongst JAX researchers, technicians and their associates. The mice they were developing became, consequently, highly characterized. This in turn served, as Rader reminds us, to "reinforce the equation of JAX mice with standard mice … it functioned as documentation but only for a specific type of software: for the information to be useful JAX mice had to be used" (Rader, 2004: 169-170).

Rader's denotation 'JAX mice' is not incidental here and neither is it simply a convenient shorthand. In 1941, Little had elected to trademark the name by which their strains had colloquially become known: JAX®Mice. Nothing is recorded of his motivations, but it

seems certain that a desire to capitalise on the reputational value of Jackson's products - these highly characterised and beautifully crafted biological works - must surely have figured highly in his thinking. JAX has always employed the brand to signify the source of origin of its mice, but now increasingly relies on it to secure and promote the reputation and integrity of Jackson's strains and the corporate identity and reputation of the laboratory itself.

There are interesting reasons for this. JAX is a non-profit entity that receives federal funding from the NIH to help it resource research endeavors (particularly those requiring rare inbred or engineered strains) at close to cost. This certainly enables them to embrace 'openness' in ways that would be economically unsustainable for rival corporate suppliers, such as Charles Rivers. Nevertheless, maintaining a commitment to the principle of allowing researchers open access to their mouse genetic resources has implications for Jackson and their mouse economy. Firstly, Jackson circulates its mice subject only to its very generous 'conditions of use' protocol. This contains no restrictions on recipients' breeding from the mice they sell them, indeed they will even sell breeding pairs. Consequently, there is nothing to prevent recipients from reproducing strains or even populations in their own laboratories or from developing patentable products from those mice, if they have the infrastructural capabilities and space to do so. Were they to, Jackson would receive no royalties or future income from those uses.

Secondly, if recipients don't subscribe to the open source commons ethos they are able to patent the strains they then develop from Jackson's germinal stock. In 2006, Japan's Central Institute for Experimental Animals (CIEA) was granted a US patent on a strain of

immunodeficient mice called NOG, which it later marketed commercially.[14] In 2008, the CIEA, rather astonishingly, bought a patent infringement case against Jackson for distributing a strain of genetically modified mouse, the NSG, that they asserted was 'equivalent' to the NOG.[15] The NSG was an unpatented engineered strain that Jackson had circulated to over 640 research institutes worldwide for experimental use. Jackson had developed their NSG mouse from their existing NOD-SCID strains. It was these strains that had been previously circulated to the CIEA where they had been crossed with other strains to produce the NOG mouse. Both the NOG and the NSG were, thus, both created from NOD-SCID strains just via different processes. Outraged by this 'property grab' the NIH instructed Jackson to counter sue, arguing that the CIEA were, in fact, the infringing party as they had developed the NOG strain from the NOD-SCID strains, elements of which the NIH had 'defensively' patented to assure open access and to prevent others from patenting and monopolizing them – a prescient move it would seem.

Besmirchment of the Brand

Such incidents reflect the difficulties Jackson has experienced in regulating the use of their resources in an open source genetic commons. How, in such circumstances could they protect the stability, reputation and integrity of their mammalian research tools and corporate brand whilst still maintaining the ability to monetise their inventions? As Stephen Hilgartner has recently argued (2017: 17-19) although knowledge-control

[14] The CIEA was intending to circulate the NOG under highly restrictive terms: purchasers were prohibited from breeding or cross-breeding them whilst extensive 'reach-through' rights controlled successive work done with the mice.
[15] For a full analysis see Abbott, 2009.

regimes such as IPR "may attempt to 'pre-package' a limited set of modes of engagement" (by, for example, normalising patent as the preferred mode of protection for biological inventions) scientific actors have often proven to be extremely adept at selectively adopting "several regimes at once, or … several regimes in succession", to advance their interests. They may also, he notes, "try to construct new knowledge-control regimes by recombining elements of existing ones – as in the well-known example of the General Public License, which uses copyright and contract law to constitute a novel "free-software" regime". In response to these challenges JAX's community of researchers began to undertake just this kind of similarly provocative ontological work. By selectively combining process patents with trademark they quietly initiated a new regime for securing reputational value, generating brand loyalty and deterring unlicensed copying, and in so doing, began to operationalise a genuinely open access economy in engineered mice.

If Jackson were not insisting that accessioned mice be patented, nor consequently receiving any percentage of royalties obtained for their use, how would it be possible for them to create a continued revenue stream from their production and distribution and thus maintain their institutional viability? The answer I, believe, lies in the value that attaches to standardisation, consistency and reputational capital in laboratory experimentation. Whilst the Betty Crocker Corporation has been able to make 'genetic drift' in their brand identity work for them in economically generative ways, for a lab such as Jackson it only poses a threat to production quality. Random variations in production introduce inconsistencies that jeopardize research experiments by making replicability complex if not impossible. Genetic drift in mutant mouse colonies occurs slowly and subtly and can be difficult to discern or control but can have extremely

serious consequences. As JAX itself notes: "inattention to the effects of genetic drift and substrain divergence can confound research conclusions making them inaccurate, misleading and sometimes, unusable".[16]

Consistency in manufacture and reliability are, therefore, the hallmarks of craftsmanship in model mouse production. JAX®Mice have these qualities and the brand has become highly valorised and valued as a consequence. How though to protect this brand from becoming besmirched by unlicensed and potentially shoddy reproduction? JAX has resolved this dilemma, which confronts all producers of trademarked works in open source economies, through the development of a unique, and (somewhat surprisingly) patented process. For while the management of the Jackson Laboratory have always been philosophically opposed to 'product patents' they are willing to accommodate what are termed 'process patents', in the interest of protecting a particular attribute or quality, one that is, in my view, becoming increasingly important in all open source and collective commons enterprises: reputation.

This process patent is for their Genetic Stability Program, which is designed to protect the integrity of the Lab's resources by limiting cumulative genetic drift. It does so by literally 'revitalizing' these strains with new genetic material. This system enables the production colonies to be literally "re-booted', as Jackson puts it, with cryogenically preserved embryos or gametes from specially prepared stocks, every five generations. This refreshment effectively 'freezes' or stabilizes the genetic profile of the mouse,

[16] https://www.jax.org/news-and-insights/jax-blog/2015/march/more-researchers-are-using-b6j-mice-than-ever-before. The imperative to create the program arose from a number of important cases in which genetic drift or substrain divergence marred research experiments (See Bailey, 1982; Threadgill et.al, 1997, Specht and Schoepfer, 2001, and Stevens et.al 2007).

"stopping the accumulation of mutations and revolutionizing the uniformity of the mouse as a research tool".[17] The stocks are set up to give a 25-year supply of genetically consistent mouse models. Process patents on the GSP technology ensure the genetic consistency and integrity of the engineered strain whilst trademark provides an assurance of the reputation of both the strains and their maker.

Product patents on strains themselves, have become, in many instances, outmoded for researchers at JAX. Although particular lines can be stabilized sufficiently to sustain such claims many scientists have come to recognize that prosecuting them will only serve to restrict their circulation, creative exchange, and use. Many have thus elected to be recognized as 'donors' to collaboratively authored open access resource repositories rather than individual 'inventors' of privately owned products. However, in forgoing the associated reach through rights to valuable strains these individuals and the Jackson itself lose access to a vital revenue stream. This proves to matter less than might be imagined, as the deft application of what Calvert (2012:183) terms a "diverse ecology of open and proprietary forms" (in this case a process patent on their Genetic Stability Program and the trademarking of strains produced and stabilized through such means) has here combined to deliver a guarantee of quality that is simply unrivalled in the mouse genetics economy. Consequently, JAX®Mice are recognized globally as the 'gold standard' mammalian mouse strains and models in the world. Donors are prepared to forgo patents on their invented models (which may actually deter use) and agree to open circulation if their model can be accessioned to a bank that will work hard to assure its continued integrity, and thus, reputational and economic value. As David

[17] https://www.jax.org/jax-mice-and-services/find-and-order-jax-mice/why-jax-mice/patented-genetic-stability-program

Einhorn puts it: "donors really appreciate the value in having their mice available from a leading mammalian genetics research institution with exceptional genetic quality control and comprehensive mouse data bases, as this package also makes the donors' mice more attractive to potential *for-profit licensees*" (my italics).[18] The guaranteed integrity and reliability of the mice, and JAX's unrivalled institutional reputation has boosted production and driven demand, turning it into a global market leader that sells over three million mutant mice per year to researchers across the world. It is by these means that it has been possible for Jackson's researchers (internal and external) to disavow product patents, meet all the ethical principles of open access to mammalian genetic resources and, in the process, create a genuinely workable mouse academic commons – whilst still generating financial returns through reputational capital.

Conclusion

One of the enduring curiosities of the emergence of open source economies is how the authors or inventors that contribute to them can both protect the integrity of the works they donate and capitalize on the value of the intellectual labour they have invested in their creation. This exact set of questions arose in relation to the emergence of a new academic research commons for mammalian genetic resources, but has to date remained largely unexplored. Throughout the first two decades of the biotechnological revolution (from the mid 1980s to the mid 2000s) the dictum that product patents were an essential tool for asserting and protecting the rights and income of inventors of engineered organisms, became not only popular, but canonical. It has therefore, been

[18] Einhorn, D. (2008) Research Report to the National Institutes of Health Grant Number 5RO3 HG003766-01 Unpublished: Courtesy of the author.

difficult to imagine, in such contexts, why the inventors of engineered model mice would give up their patent rights or agree to allow their creations to circulate freely in an open source economy.

Drawing on an analysis of research undertaken within the Jackson Laboratory, and situating that within broader theoretical discussions of craft working and the impact that patent can have on knowledge creation in a commons environment I have here demonstrated why product patents have not performed the work envisaged for them by their original advocates. In a community in which collaborative working is essential to the refinement of models and in which iterative forms of experimentation underpin the continued generation of new strains, constraining circulation to monetise the value of individual mice as 'finished products' was always, ultimately, going to have stifling effects on innovation – to the detriment of all. Model mice, including JAX®Mice are, in this context, perhaps best conceptualised as collectively authored performative works rather than as products *per se*. If we view the model mice themselves as a kind of biological commons to which many authors contribute, the value of allowing them to be 'open-sourced' as foundational resources that can be continually reinvented and refined by a wider constituency of inventors becomes more apparent.

The product, I would argue, in this particular cosmology, is not in fact the model mouse or strain itself, which we have determined can become dissolute or corrupt, but rather the experimental techniques that assure its continued integrity and thus, epistemological and economic value in laboratory settings and in the bioeconomy more generally. Process patents have been deployed to protect the means of delivering genetic stability in new mouse strains and these, coupled with trademark, together

deliver to the mouse consumer a guarantee of the reliability of the personality, identity, 'moral standing' and foremostly reputation of the protected strain. It is this assurance that is monetised within the 'open source' mouse genetics economy and which returns value to all the mouse's shareholders, whose donations together constitute the Jackson Lab's resources.

Such developments perhaps invite us to reflect finally on the question of what the re-valorisation of trademark might say, in this context, about other kinds of ontological drift – the drift for example that is evidenced in the way we conceptualise these mice. It would seem that the model mouse is now becoming 'humanised' at more than a molecular genetic level. No longer characterised simply as technological research 'tools' model mice seem now to be acquiring identities, legal personalities, reputations, and 'careers' that are singular, and require promotion and active protection from tarnishment. While the global mouse commons might create a permissive space of exchange, the model mouse should not, it seems, circulate too promiscuously within it – not, at least, without the reputational protection that a trademark can afford.

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